



LAWRENCE  
LIVERMORE  
NATIONAL  
LABORATORY

# Application of a pilot control banding tool for risk level assessment and control of nanoparticle exposures

S. Y. Paik, D. M. Zalk, P. Swuste

March 5, 2008

The Annals of Occupational Hygiene

## **Disclaimer**

---

This document was prepared as an account of work sponsored by an agency of the United States government. Neither the United States government nor Lawrence Livermore National Security, LLC, nor any of their employees makes any warranty, expressed or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States government or Lawrence Livermore National Security, LLC. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States government or Lawrence Livermore National Security, LLC, and shall not be used for advertising or product endorsement purposes.

# **Application of a pilot control banding tool for risk level assessment and control of nanoparticle exposures**

Samuel Y. Paik<sup>1</sup>, David M. Zalk<sup>1\*</sup>, and Paul Swuste<sup>2</sup>

<sup>1</sup>Lawrence Livermore National Laboratory, P.O.Box 808, L-871 Livermore California  
94551, United States

<sup>2</sup>Delft University of Technology - Safety Science Group, PO Box 5015, Delft 2600 GA,  
The Netherlands

## **ABSTRACT**

Control Banding (CB) strategies offer simplified solutions for controlling worker exposures to constituents that are found in the workplace in the absence of firm toxicological and exposure data. These strategies may be particularly useful in nanotechnology applications, considering the overwhelming level of uncertainty over what nanomaterials and nanotechnologies present as potential work-related health risks, what about these materials might lead to adverse toxicological activity, how risk related to these might be assessed, and how to manage these issues in the absence of this information. This study introduces a pilot CB tool or ‘CB Nanotool’ that was developed specifically for characterizing the health aspects of working with engineered nanoparticles and determining the level of risk and associated controls for five ongoing nanotechnology-related operations being conducted at two Department of Energy (DOE) research laboratories. Based on the application of the CB Nanotool, four of the five operations evaluated in this study were found to have implemented controls consistent with what was recommended by the CB Nanotool, with one operation even exceeding the required controls for that activity. The one remaining operation was determined to require an upgrade in controls. By developing this dynamic CB Nanotool within the realm of the scientific information available, this application of CB appears to be a useful approach for assessing the risk of nanomaterial operations, providing recommendations for appropriate engineering controls, and facilitating the allocation of resources to the activities that most need them.

*Key words:* nanotechnology, nanoparticle, nanomaterial, control banding, risk assessment, risk level, exposure control, toolkit, CB Nanotool.

\* Author to whom correspondence should be addressed. Email [zalk1@llnl.gov](mailto:zalk1@llnl.gov)

## INTRODUCTION

The traditional industrial hygiene (IH) approach to controlling exposures to harmful particles in the workplace is to measure the air concentrations of the particles of interest from the worker's breathing zone, compare those concentrations to exposure limits determined for those particles, and implement control measures to reduce concentrations below the exposure limits. This assumes the following: 1) the sampled concentrations are representative of what the worker is actually breathing; 2) the appropriate index of exposure is known; 3) analytical methods are available to quantify that index; and 4) the exposure levels at which those particles produce adverse health effects are known. If any of these is not well characterized, the measurements taken may have limited value as it would be difficult to perform a valid risk assessment. In addressing worker exposures to engineered nanoparticles, the first requirement can be satisfied by obtaining an air sample from the worker's breathing zone using a sampling pump, where forces such as particle inertia and gravity have minimal impact on the ability of the nanoparticles (defined as having 2 or 3 dimensions less than 100 nanometers (ASTM, 2007)) to follow the sampled air into the sampler since nanoparticles approach molecular size. The second requirement - an appropriate index of exposure - has not yet been satisfied for nanoparticles with no international scientific community consensus on what the relevant index of exposure is (NIOSH, 2006; ISO, 2007). For

example, a number of studies are suggesting that total surface area concentration may be a better exposure index than mass concentration (Oberdorster et al., 1994; Tran et al., 2000). Particle number concentration has also been suggested as an alternative to mass concentration (NIOSH, 2006). This lack of consensus directly affects the third requirement, since sampling and analytical methods rely on knowledge of what needs to be measured. Commercially available instruments can measure surface area concentration, number concentration, or mass concentration, but these generally measure larger particles in addition to nanoparticles, introducing potentially large biases (summarized in ISO, 2007 and NIOSH, 2006). For example, both the CPC Model 3007 (TSI, Shoreview, MN), which measures particle number concentration, and the Model 3550 Nanoparticle Surface Area Monitor (TSI, Shoreview, MN), which measures total particle surface area, measure particles up to 1000 nm in diameter, and do not have cut-offs at the upper limit of what is defined as a nanoparticle. The fourth requirement may be the largest barrier to assessing the risk of working with nanomaterials. Very little toxicological data for determining exposure limits for nanoparticles, and virtually no human studies, are available (Maynard and Kuempel, 2005). This is due to the lack of consensus on the appropriate index of exposure and the relative novelty of nanotechnology and the new materials used in this technology. Therefore, there are numerous barriers to overcome before traditional IH can produce useful data.

A plausible alternative to the traditional IH approach is the utilization of control banding (CB). Control Banding (CB) strategies offer simplified solutions for controlling worker exposures to constituents that are found in the workplace. Historical progression

has shown that CB is a framework for managing occupational risks in the face of uncertainty (summarized in Zalk and Nelson, 2008 and Money, 2003). The CB concept developed by the U.K. Health and Safety Executive (HSE) in 1999 as the COSHH Essentials model (HSE, 1999; Oldershaw, 2001), has seen widespread use in the U.K. and elsewhere. CB makes business sense because chemical companies are constantly synthesizing new chemicals, and developing occupational exposure limits for all experimental chemicals is not feasible as most will never become commercialized. This very aspect of decision-making based on incomplete information makes CB an attractive option for controlling nanoparticle exposures.

Like its counterparts in the pharmaceutical and microbiological industries, the nanotechnology industry also has to achieve a risk management program with an insufficient basis for traditional IH quantitative risk assessment approaches. While nanotechnologies show incredible promise in such areas as materials science, cancer treatment, and environmental remediation, they have created a heightened level of concern for research and development (R&D) and manufacturing workers due to the overwhelming level of uncertainty over what nanomaterials and nanotechnologies present as potential work-related health risks, what about these materials might lead to adverse toxicological activity, how risk related to these might be assessed, and how to manage these issues in the absence of this information (Maynard, 2007). In theory, CB has been proposed as a practical approach to address exposure to nanoparticles and achieving exposure control in the absence of this data (Zalk and Nelson, 2008; Schulte et al., 2008; Maynard, 2007; and Nelson et al, 2007). A conceptual CB model was presented by

Maynard (2007) which offers the same four control approaches of the COSHH Essentials model as stratified by corresponding ‘impact’ and ‘exposure’ indices. This model combines engineered nanomaterial composition parameters (shape, size, surface area, and surface activity) with their exposure availability (dustiness and amount in use) and links these indices to bands with corresponding control approaches. This model is presented in a historical progression of pragmatic approaches to exposure control considered a complement to traditional IH risk assessment.

## OBJECTIVE

While CB appears to be an appropriate methodology for controlling exposures to nanomaterials in concept, very few, if any, comprehensive tools are currently available for ongoing nanotechnology operations. The goal of this study, therefore, was to further explore the feasibility of using CB for controlling exposures to nanomaterials by developing and introducing a pilot CB tool or ‘CB Nanotool’ based on existing knowledge of nanomaterial toxicology and utilizing the CB framework proposed in earlier publications. As part of this effort, the CB Nanotool was used to determine the risk and controls associated with five ongoing operations at two Department of Energy (DOE) research laboratories.

## METHODS

This study can be divided into two phases: 1) development of the CB Nanotool for nanotechnology operations; and 2) application of the tool to determine risk levels and controls for five different operations.

#### Development of the CB Nanotool for nanotechnology operations

Maidment (1998) stressed the importance of limiting the number of factors in the CB model to reduce its complexity and increase its applicability for non-experts. To achieve this balance of simplicity and effectiveness, Maidment suggested four categories, or “bands”, to assist in preventing exposure to chemicals. These four control strategies are a grouping of three levels of engineering controls based on sound IH principles, with professional IH expertise as a fourth category. The control band for a particular operation is based on the overall risk level (RL) determined for that operation. The RL is determined by a ‘severity’ score and a ‘probability’ score, which are analogous to the ‘impact’ index and ‘exposure’ index described in Maynard (2007). The biggest challenge in developing any pilot CB tool is deciding how these scores are to be determined. Fig 1 provides the matrix for overall RL determination.



(Insert FIGURE 1)

This matrix is similar to that used in the implementation of CB through the HSE's COSHH Essentials program (HSE, 1999; Garrod and Rajan-Sithamparanadarajah, 2003); however, for simplicity, it contains one less column and row in line with comparable model development parameters (Maidment 1998). It should be noted that for several of the factors described below, 0 points were assigned to the lowest rating for a given factor. This does not in any way imply that no adverse health effects are anticipated at these levels; the 0 points were assigned as an indication of low 'relative' severity or probability.

#### Severity Determination

It was anticipated early in the development of this tool that for many of the factors that are considered important for determining the severity score, the information for that factor would not be known due to the reasons stated above. While the most conservative approach would be to treat an unknown hazard as equivalent to a high hazard, the authors felt this was over-conservative and would likely place an unnecessary burden on those managing the work. For this reason, it was decided that when the information for a given factor was "Unknown", 75% of the point value of "High" would be given for that factor. What this translates to is that for a hypothetical nanotechnology operation for which

nothing was known (other than it involves nanoparticles), the resulting RL would be “RL3” and the required control would be “Containment”. In this scenario, if just one rating for any of the factors was later determined to be “High”, with all other ratings remaining as “Unknown”, the tool would assign this activity as “RL4” and require the maximum control.

Based on what is known about the toxicological effects of nanoparticles in the current literature, the authors believe the following are factors that should be considered in determining the overall severity of the nanoscale materials. While it is recognized that different groups may disagree on what the most important factors are, the intent of the CB Nanotool was to account for all the major factors that the current literature suggests is important in determining nanomaterial toxicity. These factors influence the ability of particles to reach the respiratory tract, their ability to deposit in various regions of the respiratory tract, their ability to penetrate or be absorbed through skin, and their ability to elicit biological responses. It was recognized that particles entering the respiratory tract can cause adverse effects by remaining in the respiratory tract (primarily the lungs) or by entering the blood circulation.

1. *Surface chemistry.* Surface chemistry is known to be a key factor influencing the toxicity of inhaled particles (Maynard and Kuempel, 2005). Crystalline silica, for example, elicits a much stronger response than titanium dioxide, even when normalized for surface area or mass. Particle surface free radical activity is the primary factor that influences the material’s overall surface reactivity. Research

studies should be consulted, when available, to make a judgment of whether the surface reactivity of the nanomaterial is high, medium, or low. For example, free radical activity is associated with the generation of reactive oxygen species and oxidative stress responses in the lungs. Reactive oxygen species and oxidative stress responses can be quantified by analyzing the bronchoalveolar lavage fluid (BALF) from rats used in toxicological studies. The BALF may be analyzed for markers of inflammation, levels of pulmonary oxidants, antioxidant status, and markers of lung tissue damage (Albrecht et al., 2005). These types of information need to be consulted in determining the surface reactivity of the nanomaterial. A rating of “High” results in 10 points; a rating of “Medium” results in 5 points; a rating of “Low” results in 0 points; and a rating of “Unknown” results in 7.5 points.

2. *Particle shape.* Studies have shown that exposure to fibrous particles like asbestos have long been associated with increased risk of fibrosis and cancer (Doll, 1955). Tubular structures, like carbon nanotubes, have also been shown to cause inflammation and lesions in rat lungs (Lam et al., 2004). Based on this information, the highest severity score is given to fibrous or tubular-shaped particles. Particles with irregular shapes (other than tubular or fibrous) are given a medium severity score because they typically have higher surface areas relative to isotropic (e.g. compact or spherical particles) particles. A rating of “Tubular or fibrous” results in 10 points; a rating of “Anisotropic” results in 5 points; a rating

of “Compact or spherical” results in 0 pts; and a rating of “Unknown” results in 7.5 points.

3. *Particle diameter.* Based on the particle deposition model developed by the International Commission of Radiological Protection (ICRP, 1994), particles in the 1-10 nm range have a greater than approximately 80% chance of depositing in the respiratory tract. Particles in the 10-40 nm range have a greater than approximately 50% possibility of depositing in the respiratory tract and particles in the 41-100 nm range have a greater than approximately 20% possibility of depositing in the respiratory tract. Since deposition is the first step in producing potential adverse health effects, regardless of which region of the respiratory tract the particles deposit in, the severity score was based on the particles’ ability to deposit anywhere in the respiratory tract. Based on this modeling, a rating of “1-10 nm” results in 10 points; a rating of “11-40 nm” results in 5 points; a rating of “<41-100 nm” results in 0 points; and a rating of “Unknown” results in 7.5 points.
4. *Solubility.* A number of studies have shown that poorly soluble inhaled nanoparticles can cause oxidative stress, leading to inflammation, fibrosis, or cancer (Castranova, 1998; Donaldson et al, 1998). Since soluble nanoparticles can also cause adverse effects through dissolution in the blood, severity points are assigned to soluble nanoparticles as well, but to a lesser degree than for insoluble particles. A rating of “Insoluble” results in 10 points; a rating of “Soluble” results

in 5 points; and a rating of “Unknown” results in 7.5 points.

5. *Carcinogenicity*. Points are assigned based on whether the nanomaterial is carcinogenic or not, regardless of whether the material is a human or animal carcinogen. Very few nanomaterials (e.g., titanium dioxide) have been identified as potential carcinogens (IARC, 2006). A rating of “Yes” results in 7.5 points; a rating of “No” results in 0 points; and a rating of “Unknown” results in 5.625 points.
6. *Reproductive toxicity*. Points are assigned based on whether the nanomaterial is a reproductive hazard or not. This information is not readily available for most nanomaterials. A rating of “Yes” results in 7.5 points; a rating of “No” results in 0 points; and a rating of “Unknown” results in 5.625 points.
7. *Mutagenicity*. Points are assigned based on whether the nanomaterial is a mutagen or not. This information is not readily available for most nanomaterials. A rating of “Yes” results in 7.5 points; a rating of “No” results in 0 points; and a rating of “Unknown” results in 5.625 points.
8. *Dermal toxicity*. Points are assigned based on whether the nanomaterial is a dermal hazard or not. This is understood to encompass both dermal absorption and cutaneous toxicity. This information is not readily available for most

nanomaterials. A rating of “Yes” results in 7.5 points; a rating of “No” results in 0 points; and a rating of “Unknown” results in 5.625 points.

9. *Toxicity of parent material.* The bulk materials of some nanoparticles have established occupational exposure limits. While it is known that the toxicity of particles at the nanoscale can differ significantly from their larger counterparts, this provides a good starting point for understanding the toxicity of the material. Points are assigned according to the OEL band of the bulk material. A rating of “0-10  $\mu\text{g}/\text{m}^3$ ” results in 10 points; a rating of “11-100  $\mu\text{g}/\text{m}^3$ ” results in 5 points; a rating of “>100  $\mu\text{g}/\text{m}^3$ ” results in 2.5 points; and a rating of “Unknown” results in 7.5 points.
10. *Carcinogenicity of parent material.* Points are assigned based on whether the parent material is carcinogenic or not. A rating of “Yes” results in 5 points; a rating of “No” results in 0 points; and a rating of “Unknown” results in 3.75 points. The National Toxicology Program, International Agency for Research on Cancer, and the American Conference of Governmental Industrial Hygienists provide lists of suspected and confirmed human carcinogens.
11. *Reproductive toxicity of parent material.* Points are assigned based on whether the parent material is a reproductive hazard or not. A rating of “Yes” results in 5 points; a rating of “No” results in 0 points; and a rating of “Unknown” results in 3.75 points.

12. *Mutagenicity of parent material.* Points are assigned based on whether the parent material is a mutagen or not. A rating of “Yes” results in 5 points; a rating of “No” results in 0 points; and a rating of “Unknown” results in 3.75 points.

13. *Dermal hazard potential of parent material.* Points are assigned based on whether the parent material is a dermal hazard or not. As stated before, this is understood to encompass both dermal absorption and cutaneous toxicity. A rating of “Yes” results in 5 points; a rating of “No” results in 0 points; and a rating of “Unknown” results in 3.75 points.

A number of studies show that the particle surface area is closely associated with lung responses, including tissue damage and inflammation in rat lungs (Oberdorster et al., 1994; Tran et al., 2000). This factor is accounted for by assigning higher severity scores to smaller particles (which would have a higher surface area compared to larger particles at the same mass concentration) and anisotropic particles (which generally would have higher surface-to-volume ratios). This factor is also accounted for by assigning higher probability scores to operations that have higher “dustiness” levels (see next section), which would invariably have higher overall surface area concentrations relative to operations with lower dustiness levels.

The overall severity score is determined based on the sum of all the points from the severity factors. The maximum score is 100. Since nanoparticles usually behave

much differently than their parent material due to their small scale, which is what makes engineered nanoparticles so useful and potentially much more toxic, greater consideration was given to the nanomaterial characteristics (70 possible points out of 100) than to the parent material characteristics (30 possible points out of 100). Since the parent material and nanomaterial are both considered in determining the severity score, it should be understood that the parent material ratings should not influence the ratings that are given for the same factor at the nanoscale (e.g., carcinogenicity), i.e., each factor should be rated independently of another. An overall severity score of 0-25 was considered low severity; an overall severity score of 26-50 was considered medium severity; an overall severity score of 51-75 was considered high severity; and an overall severity score of 76-100 was considered very high severity.

#### Probability Determination

In order to determine a probability score that can be combined with the severity score to determine the overall RL of the operation, the authors believe the following factors should be considered when determining the overall probability score. These factors determine the extent to which employees may be potentially exposed to nanoscale materials. The probability score is based on the potential for nanoparticles to become airborne. This primarily affects exposure by inhalation; however, it also influences the potential for dermal exposure because the likelihood of skin contact with the nanomaterials increases with more nanoparticles becoming airborne and depositing on work surfaces.



1. *Estimated amount of nanomaterial used during task.* When all else is constant, the amount of the nanomaterial used during an operation increases the likelihood of the material being available to interact with the user. For nanomaterials embedded on substrates or suspended in liquids, the amount should be based only on the nanomaterial component itself, not to include the substrate or liquid portion. Therefore, points are assigned based on the total amount of nanomaterial used during a single operation. A rating of “>100 mg” results in 25 points; a rating of “11-100 mg” results in 12.5 points; a rating of “0-10 mg” results in a rating of 6.25 points; and a rating of “Unknown” results in 18.75 points.
2. *Dustiness/mistiness.* Since employees are potentially exposed to nanoparticles in either dry or wet form, this factor encompasses both dustiness and/or mistiness of the nanomaterial. For the same mass concentration, however, non-agglomerated dry nanoparticles should be given a higher dustiness/mistiness rating than agglomerated or liquid-suspended nanoparticles. While not required, quantitative measurement devices would be particularly useful in determining the dustiness/mistiness level. A condensation nuclei counter that provides number concentration, for example, would provide insight into the overall dustiness level. Knowledge of the operation (e.g., handling dry powders versus liquid suspensions of nanoparticles) and observation of work surfaces (e.g., cleanliness of surfaces pre- and post- handling of nanomaterials) would be another means to qualitatively estimate dustiness/mistiness. Due to the size of nanomaterials, visibility may not be a reliable means to estimate overall dustiness/mistiness. Until further guidance is

provided on the appropriate means to quantify exposure to nanoparticles, points will be assigned based on an estimate of 'relative' dustiness/mistiness level. One design feature of the CB Nanotool is that a rating of "None" for dustiness/mistiness level (and only for this factor) automatically causes the overall probability score to be "Extremely Unlikely", regardless of what the other probability factors are, since the other factors will not be relevant if no dust or mist is being generated. Examples of operations that would result in a "None" rating are handling of carbon nanotubes embedded on fixed substrates and working with non-agitated liquid suspensions. This feature was specifically incorporated into the tool for this reason and represents the only departure from the 'rules' that govern the tool. The dustiness/mistiness factor is the most important one in determining the overall probability score, and as such, relatively high numbers of points are assigned to the ratings in this category. A rating of "High" results in 30 points; a rating of "Medium" results in 15 points; a rating of "Low" results in 7.5 points; a rating of "None" results in 0 points; and a rating of "Unknown" results in 22.5 points.

3. *Number of employees with similar exposure.* For this factor, points are assigned according to the number of employees assigned to this activity. With higher numbers of employees engaged in the activity, there is a higher probability of employees being exposed. A rating of ">15" employees results in 15 points; a rating of 11-15 points results in 10 points; a rating of "6-10" results in 5 points; a

rating of “1-5” results in 0 points; and a rating of “Unknown” results in 11.25 points.

4. *Frequency of operation.* Points are assigned based on the frequency of the operation, as more frequent operations are more likely to result in employee exposures. A rating of “Daily” results in 15 points; a rating of “Weekly” results in 10 points; a rating of “Monthly” results in 5 points; a rating of “Less than monthly” results in 0 points; and a rating of “Unknown” results in 11.25 points.
5. *Duration of operation.* Points are assigned based on the duration of the operation, as longer operations are more likely to result in employee exposures. A rating of “>4 hours” results in 15 points; a rating of “1-4 hours” results in 10 points; a rating of “30-60 min” results in 5 points; a rating of “Less than 30 min” results in 0 points; and a rating of “Unknown” results in 11.25 points.

The overall probability score is based on the sum of all the points from the probability factors. The maximum score is 100. An overall probability score of 0-25 was considered extremely unlikely; an overall probability score of 26-50 was considered less likely; an overall probability score of 51-75 was considered likely; and an overall probability score of 76-100 was considered probable.

(Insert TABLE 1)

Based on the severity score and probability score for an operation, the overall RL and corresponding control band is determined by the matrix shown previously in Figure 1.

#### Application of the CB Nanotool for five different operations.

In order to pilot test the CB Nanotool, information was gathered from five different operations in two DOE research laboratories. Four operations are being performed at the Lawrence Livermore National Laboratory (LLNL) and one operation was performed at the Stanford Linear Accelerator Center (SLAC). A nanotechnology information field-based form was developed to appropriately collect data. Field visits were initiated at LLNL through the cognizant IHs for those operations with principal researchers participating in reviews. The field visit at SLAC was initiated by their ES&H

Division Office and principal researchers for their operation participated in the review along with ES&H Division staff.

## RESULTS

Operation descriptions are summarized below, mostly in general terms, and the results of the CB Nanotool are shown in the appendix.

### Synthesis of nanoporous metal foams (Activity 1)

Nanoporous metal foams are synthesized by mixing metal nanoparticles with polystyrene spheres and water. These components are weighed and combined into a vial inside a glove box and the mixture is transported to a sonicator. After sonication is complete, the sample is pipetted into a tube where water is removed from the sample using a water-absorbing medium. Once the sample is removed from the tube, it is placed inside a furnace and the polystyrene spheres are vaporized, producing a nanoporous metal foam. Based on knowledge of the nanomaterial characteristics and a thorough review of the operation in the field, the CB tool indicated that the overall RL was 3. The required engineering control, therefore, would be containment. The portion of the activity that had the highest likelihood of exposure was during the initial weighing and mixing phase, and this was performed inside a glove box with a HEPA-filtered exhaust system. The current controls, therefore, were consistent with what was recommended from the CB Nanotool.

### Flame synthesis of ceramic nanoparticles (Activity 2)

Ceramic nanoparticles (e.g., lutetium oxide, lutetium aluminum garnet) are synthesized by injecting carrier liquids into a flame inside a fume hood which are consumed through combustion. The resulting nanoparticles are produced and collected onto a filter plate. Based on knowledge of the ceramic nanoparticle characteristics and a thorough review of the operation, the CB Nanotool indicated that the overall RL was 2. The required engineering control, therefore, would be a fume hood or local exhaust ventilation, which was in fact what was utilized during this operation.

### Synthesis of carbon nanotubes (Activity 3)

Carbon nanotubes are synthesized by passing a mixture of an inert carrier gas (Ar), hydrogen, and hydrocarbon precursor gas (e.g., ethylene, acetylene) over catalyst particles deposited on silicon substrates within a horizontal tube furnace. Trace amounts of water are added to the gas mixture to enhance the growth process. The carbon nanotubes are fully attached to the substrates when they are removed from the tube furnace using forceps. The samples are then transferred into plastic containers for further characterization. Based on knowledge of the carbon nanotube characteristics and a thorough review of the operation in the field, the CB Nanotool indicated that the overall RL was 2. The required engineering control, therefore, would be a fume hood or local exhaust ventilation. In this particular operation, the carbon nanotubes were synthesized within an enclosed tube furnace and therefore the level of control achieved was

containment. This level exceeded the required control as determined from the CB Nanotool.

#### Consolidation of ceramic nanoparticles (Activity 4)

Ceramic nanoparticles are weighed inside a chemical fume hood. An organic solvent (e.g., ethanol) is added to the powder mixture inside a ball mill jar and milled for several hours. The mixture is pressed into a die inside the fume hood and the compacted material is heated in a burn oven inside the fume hood to remove the organics and other residues. The material is then sintered inside a vertical tube furnace and quenched as it is dropped into a bucket located below the furnace. The cooled material is transferred into a plastic container. Based on knowledge of the ceramic nanoparticle characteristics and a thorough review of the operation in the field, the CB Nanotool indicated that the overall RL was 3. The required engineering control, therefore, would be containment. A fume hood, in fact, was used throughout this operation; therefore, the level of control was not adequate and would need to be upgraded.

#### Preparation of a single dry bacteriogenic uranium dioxide sample (Activity 5)

A sample of uranium dioxide in a container is opened inside an anaerobic chamber. The sample is allowed to dry out inside the chamber and then transferred into

a vanadium metal canister for shipment to another research facility. Based on knowledge of the uranium dioxide nanoparticle characteristics and a thorough review of the operation, the CB Nanotool indicated that the overall RL was 3. The required engineering control would be containment. The current controls, therefore, were consistent with what was recommended from the CB Nanotool, as all the operations were performed inside an enclosed chamber with HEPA filtered exhaust.

## DISCUSSION

The understanding of structure- *and* chemistry-related health effects from exposures within all aspects of the nanoparticle technology industries comes together into a burgeoning toxicological research field. Traditional IH sampling for nanoparticles at this point in time may very well miss an appropriate exposure index unless a complete collection of associated number, surface area, and mass concentrations is simultaneously measured. The stratification of health risk within professional IH teachings begins to lose footing when the appropriate toxicological endpoint, biologically available concentrations, and its effective dose potential are not fully understood. From the practical aspect of protecting the worker as a primary objective, the toxicological “wait and see” approach begins to lose ground to the “band and control” method of primary prevention.

The CB approach for controlling nanoparticle exposure is given leeway from its most popular requestor. In order to work safely with nanomaterials, Maynard has said



that existing IH “will get us 60 to 70 percent of the way”, leaving “a gap that has to be filled with this strategic, targeted research” (Cable, 2006). CB offers a method to bridge this gap while remaining dynamic in adjusting to new, available research. While the determination of severity and probability were dependent on factors that are known or suspected to be important in characterizing risk from nanoparticle exposure, the relative importance of one factor compared to another may change as more knowledge on the adverse effects of nanoparticles becomes available. Ranges of values corresponding to discrete scores given for each factor may also be modified according to the level of risk one is willing to accept and ranges of values relevant to the organization utilizing the tool. Thus, some level of expert judgment should be used to ensure recommended controls produced from the CB Nanotool are in fact the most appropriate for the activity in question. In this study, the ranges of values used in the CB Nanotool correspond to those ranges that one would expect in small-scale research-type operations. For large-scale manufacturing of nanoparticles, ranges of values may be quite different than those utilized for small-scale R&D work, particularly with respect to the probability factors’ ranges. Large-scale manufacturing processes also typically involve several steps, each of which would likely need to be assessed as a separate line item using the tool.

The CB Nanotool was developed in a Microsoft Excel® spreadsheet allowing automatic RL calculations and corresponding control band based on the operational review. While this tool can be used without obtaining specific field measurements, the tool can be used in conjunction with quantitative measurements as they become available. For example, dustiness may eventually be defined in terms of overall particle surface area

or particle number and be measurable. The CB Nanotool therefore is dynamic and can potentially be utilized as effective measurement techniques become available. It should be recognized, however, that any CB tool, must be used with some degree of caution. The different factors considered, weighted, and influencing the overall RL and control band are determined as educated ‘guesses’ as to factor importance and range delineation. Any CB tool utility requires frequent use, validation, and evaluation of recommended control effectiveness. The authors, therefore, strongly encourage the further utilization of this or other similar tools for a wide range of applications as these efforts will undoubtedly improve and refine the tool.

## CONCLUSION

With investment increasing the global value of nanotechnology products to 2.5 trillion dollars by 2014 (Lux Research, 2004), health and safety professionals must strive to protect employees involved in technological development and product manufacture, as well as eventual consumers. Engineering controls remain the most important and effective means for preventing or limiting employee exposures. Based on the application of the CB Nanotool, four of the five operations evaluated in this study were found to have implemented controls consistent with what was recommended by the CB Nanotool, with one operation even exceeding the required controls for that activity. The one remaining operation was determined to require an upgrade in controls. The fact that the CB Nanotool produced recommendations that were largely consistent with the IH expert opinions that dictated the existing controls can be viewed as a further validation of the

CB Nanotool. By developing this dynamic CB Nanotool within the realm of scientific information available, this application of CB appears to be a useful approach for assessing the risk of nanomaterial operations, providing recommendations for appropriate engineering controls, and facilitating appropriate resource allocations.

## ACKNOWLEDGMENTS

This work was performed under the auspices of the U.S. Department of Energy by Lawrence Livermore National Laboratory under Contract DE-AC52-07NA27344. The authors would like to thank the Stanford Linear Accelerator Center for providing a venue for one of the nanotechnology operation reviews. The authors would like to acknowledge Remko Houba for his expertise and review, and Zak Islam, Janeen Robertson, Jennifer Kapp, Octavio Cervantes, Joshua Kuntz, Aleksandr Noy, and Howard Hoyt for their assistance in the activity reviews.

## REFERENCES

- ASTM International (2007) *Terminology for Nanotechnology*. West Conshohocken, PA: ASTM International, E2456-06.
- Cable, J. (2006). Nanotech expert calls for more investment in EHS research. *Occupational Hazards*, November 2006.
- Castranova, V. (1998) Particles and the airways: Basic biological mechanisms of pulmonary pathogenicity. *Applied Occupational and Environmental Hygiene*; 13(8): 613-616.
- Doll, R. (1955) Mortality from lung cancer in asbestos workers. *British Journal of Industrial Medicine*; 12:81-86.
- Donaldson, K, Li, X, and MacNee, W. (1998). Ultrafine (nanometer) particle mediated lung injury. *Journal of Aerosol Science*; 29(5-6): 553-560.
- Garrod, A and Rajan-Sithamparanadarajah, R. (2003) Developing COSHH essentials: dermal exposure, personal protective equipment and first aid. *Annals of Occupational Hygiene*; 47:577-588.
- HSE (1999) Health and Safety Executive, COSHH Essentials. London, U.K.: HSE.
- ICRP (1994) *Human respiratory tract model for radiological protection*. International Commission of Radiological Protection Publication 66.
- International Agency for Research on Cancer (2006) Titanium dioxide (IARC Group 2B), Summary of data reported, Feb. 2006.
- International Organization for Standardization (2007) *Workplace atmospheres – Ultrafine, nanoparticle and nano-structured aerosols – Inhalation exposure characterization and assessment*, ISO/TR 27628:2007(E).
- Lam, C, James, J, McCluskey, R and Hunter, R. (2004) Pulmonary toxicity of single-walled carbon nanotubes in mice 7 and 90 days after intratracheal instillation. *Toxicological Sciences*; 77: 126-134.
- Lux Research (2004) Sizing nanotechnology's value chain. New York, NY: Lux Research Inc.
- Maidment, SC. (1998) Occupational hygiene considerations in the development of a structured approach to select chemical control strategies. *Annals of Occupational Hygiene*; 42:391-400.

Maynard, A. (2007) Nanotechnology: The next big thing, or much ado about nothing? *Annals of Occupational Hygiene*; 51(1): 1-12.

Maynard, A and Kuempel, E. (2005) Airborne nanostructured particles and occupational health. *Journal of Nanoparticle Research*; 7: 587-614.

Money, C. (2003) European experiences in the development of approaches for the successful control of workplace health risks. *Annals of Occupational Hygiene*; 47, 533-540.

National Institute for Occupational Safety and Health (2006) *Approaches to Safe Nanotechnology: An Information Exchange with NIOSH*. Version 1.1.

Nelson, D., Chiusano, S., Bracker, A., Erickson, L., Geraci, C., et al. (2007). Guidance for conducting control banding analyses. AIHA Guideline 9 – 2007, AEAG07-726.

Oberdorster, G, Ferin, J, and Lehnert, B. (1994) Correlation between particle-size, in-vivo particle persistence, and lung injury. *Environmental Health Perspectives*; 102 (S5): 173-179.

Oldershaw, P. (2001) Control banding – a practical approach to judging control methods for chemicals. *Journal of Preventive Medicine*; 9: 52-58.

Schulte, P., Geraci, C., Zumwalde, R., Hoover, M., and Kuempel, E. (2008) Occupational risk management of engineered nanoparticles. *Journal of Occupational and Environmental Hygiene*; 5(4): 239-249.

Tran, C, Buchanan, D, Culen, R, Searl, A, Jones, A and Donaldson, K. (2000) Inhalation of poorly soluble particles. II. Influence of particle surface area on inflammation and clearance. *Inhalation Toxicology*; 12(12): 1113-1126.

Zalk, DM and Nelson, DI. (2008). History and evolution of Control Banding: A Review. *Journal of Occupational and Environmental Hygiene*; 5(5): 330-346.

Figure 1. Risk level (RL) matrix as a function of severity and probability.

Control bands are based on overall RL.

|          |                       | Probability                     |                        |                      |                         |
|----------|-----------------------|---------------------------------|------------------------|----------------------|-------------------------|
| Severity |                       | Extremely Unlikely<br>(0 to 25) | Less Likely<br>(26-50) | Likely<br>(51 to 75) | Probable<br>(76 to 100) |
|          | Very High<br>(76-100) | RL 3                            | RL 3                   | RL 4                 | RL 4                    |
|          | High<br>(51-75)       | RL 2                            | RL 2                   | RL 3                 | RL 4                    |
|          | Medium<br>(26-50)     | RL 1                            | RL 1                   | RL 2                 | RL 3                    |
|          | Low<br>(0-25)         | RL 1                            | RL 1                   | RL 1                 | RL 2                    |

Control bands:

RL 1: General Ventilation

RL 2: Fume hoods or local exhaust ventilation

RL 3: Containment

RL 4: Seek specialist advice

Table 1. Severity and Probability Factors and Maximum Points Per Factor  
(NM: Nanomaterial; PM: Parent Material)

| <b>Severity Factor</b>                    | <b>Maximum Pts</b> | <b>Maximum Severity Score</b>    |
|---|--------------------|----------------------------------|
| Surface Chemistry (NM)                    | 10                 | 100                              |
| Particle Shape (NM)                       | 10                 |                                  |
| Particle Diameter (NM)                    | 10                 |                                  |
| Solubility (NM)                           | 10                 |                                  |
| Carcinogenicity (NM)                      | 7.5                |                                  |
| Reproductive Toxicity (NM)                | 7.5                |                                  |
| Mutagenicity (NM)                         | 7.5                |                                  |
| Dermal Toxicity (NM)                      | 7.5                |                                  |
| Toxicity (PM)                             | 10                 |                                  |
| Carcinogenicity (PM)                      | 5                  |                                  |
| Reproductive Toxicity (PM)                | 5                  |                                  |
| Mutagenicity (PM)                         | 5                  |                                  |
| Dermal Hazard Potential (PM)              | 5                  |                                  |
| <b>Probability Factor</b>                 | <b>Maximum Pts</b> | <b>Maximum Probability Score</b> |
| Estimated Amount of Nanomaterial          | 25                 | 100                              |
| Dustiness/Mistiness                       | 30                 |                                  |
| Number of Employees With Similar Exposure | 15                 |                                  |
| Frequency of Operation                    | 15                 |                                  |
| Duration of Operation                     | 15                 |                                  |

APPENDIX. The Control Banding Nanotool applied to five activities.

Row 1 in Table A1 corresponds to Row 1 in Tables A2 to A4, and similarly with the other rows.

Table A1. The activities.

| Activity Number | Scenario Description (free text)  | Name or description of nanomaterial   | CAS#  | Activity classification                   | Current Engineering Control            |
|-----------------|---|---|---|---|--|
| 1               | Synthesis of metal foams by mixing metal nanoparticles with polystyrene latex nanoparticles in DI water. Dry powders are weighed inside glovebox and mixed with other nanoparticles inside plastic container.             | Metal nanoparticles (Cu, Ni, Ag), polystyrene latex nanoparticles   | Ni: 7440-02-0, Cu: 7440-50-8, Ag: 7440-22-4 | Handling nanoparticles in powder form     | Containment                            |
| 2               | Flame synthesis of ceramic nanoparticles. Carrier liquids are injected into a flame inside the fume hood and consumed through combustion. Small particles are synthesized and collected onto a filter plate using a pump. | Ceramic particles of Lu <sub>2</sub> O <sub>3</sub> and LuAG  | N/A   | Generating nanoparticles in the gas phase | Fume hood or local exhaust ventilation |
| 3               | Synthesis of carbon nanotubes onto substrates within a tube furnace   | Carbon nanotubes  | N/A   | Generating nanoparticles in the gas phase | Containment                            |
| 4               | Consolidation of ceramic nanoparticles  | Ceramic nanoparticles, including boron carbide, alumina, zirconia, magnesium oxide, calcium oxide, and carbo wax. | Various                                     | Handling nanoparticles in powder form     | Fume hood or local exhaust ventilation |
| 5               | Preparation/drying of uranium dioxide sample  | Uranium Dioxide   | 1344-57-6                                   | Handling nanoparticles in powder form     | Containment                            |



Table A2. Severity Factor of the parent material

| Activity<br>Number | Lowest<br>OEL<br>(mcg/m3) | Parent material |                         |          |                   |
|--------------------|---------------------------|-----------------|-------------------------|----------|-------------------|
|                    |                           | carcinogen?     | reproductive<br>hazard? | mutagen? | dermal<br>hazard? |
| 1                  | 10                        | Yes             | No                      | No       | Yes               |
| 2                  | Unknown                   | No              | No                      | No       | No                |
| 3                  | 2000                      | No              | No                      | No       | No                |
| 4                  | Unknown                   | No              | No                      | No       | No                |
| 5                  | 200                       | Unknown         | Unknown                 | Unknown  | Yes               |

Table A3. Severity Factor of the nanomaterial

| Activity Number | Surface reactivity | Particle shape       | Particle diameter (nm) | Nanoscale material |             |                      |          |                | Severity score | Severity band |
|-----------------|--------------------|----------------------|------------------------|--------------------|-------------|----------------------|----------|----------------|----------------|---------------|
|                 |                    |                      |                        | Solubility         | carcinogen? | reproductive hazard? | mutagen? | dermal hazard? |                |               |
| 1               | Unknown            | Compact or spherical | 1-10 nm                | Insoluble          | Unknown     | Unknown              | Unknown  | Unknown        | 65             | High          |
| 2               | Unknown            | Compact or spherical | > 40 nm                | Unknown            | Unknown     | Unknown              | Unknown  | Unknown        | 45             | Medium        |
| 3               | Unknown            | Tubular or fibrous   | 1-10 nm                | Insoluble          | Unknown     | Unknown              | Unknown  | Unknown        | 60             | High          |
| 4               | Unknown            | Compact or spherical | 1-10 nm                | Insoluble          | Unknown     | Unknown              | Unknown  | Unknown        | 57.5           | High          |
| 5               | Unknown            | Compact or spherical | 1-10 nm                | Insoluble          | Unknown     | Unknown              | Unknown  | Unknown        | 66.25          | High          |

Table A4. Probability Band, Risk Level, and Recommended Control

| Activity Number | Estimated maximum amount of chemical used in one day (mg) | Dustiness | Number of Employees with Similar Exposure | Frequency of Operation (annual) | Operation Duration (per shift) | Probability score | Probability band   |
|-----------------|---|-----------|---|---------------------------------|--------------------------------|-------------------|--------------------|
| 1               | 400   | High      | 1-5                                       | Weekly                          | 1-4 hr                         | 75                | Likely             |
| 2               | 4000  | High      | 1-5                                       | Weekly                          | 1-4 hr                         | 75                | Likely             |
| 3               | 50000   | None      | 11-15                                     | Weekly                          | 1-4 hr                         | 55                | Extremely Unlikely |
| 4               | 60000   | High      | 1-5                                       | Weekly                          | 1-4 hr                         | 75                | Likely             |
| 5               | 600   | High      | 1-5                                       | Yearly                          | 1-4 hr                         | 65                | Likely             |

| Overall Risk Level Without Controls | Recommended Engineering Control Based on Risk Level | Upgrade Engineering Control? |
|-------------------------------------|---|------------------------------|
| <b>RL3</b>                          | Containment   | No                           |
| <b>RL2</b>                          | Fume hood or local exhaust ventilation              | No                           |
| <b>RL2</b>                          | Fume hood or local exhaust ventilation              | No                           |
| <b>RL3</b>                          | Containment   | Yes                          |
| <b>RL3</b>                          | Containment   | No                           |